Reviewer's report

Title: Influence of calcification on the mechanical stability of plaque in three-dimensional carotid bifurcation model

Version: 2 Date: 5 December 2011

Reviewer: Konstantinos Toutouzas

Reviewer's report:

GENERAL
We have carefully considered the manuscript entitled ‘Influence of calcification on the mechanical stability of plaque in three-dimensional carotid bifurcation model’ for possible publication. The paper is well written and deals with an important topic.

MAJOR COMPULSORY REVISIONS

Comment 1: 2.2 Plaque rupture mechanics.
‘A two-dimensional modelling platform for calibrating the extent of plaque rupture based on mechanical parameters governing the atherosclerotic configuration.’
The authors should explain in more details or change the sentence since it is rather confusing and gives no specific data.

Comment 2: 2.2 Plaque rupture mechanics.
Please explain what you mean by patient-specific cases.

Comment 3: 2.2 Plaque Rupture Mechanics
You mention 65µm is the threshold for plaque rupture. However, in your experiments you talk about carotid arteries. There are resent data that suggest that TCFA in carotids is defined as cap thickness < 200µm.

Comment 4: 2.5.1 Geometry Reconstruction and Meshing
‘3D geometric model reconstruction based on realistic geometry which is used by (Tada et al., 2005)50 was performed for modelling of healthy carotid bifurcation (Fig 6).’ You state about healthy carotid bifurcation, nonetheless, in the actual figure 6 and its legend you talk about plaque in the bifurcation. There needs to be clarification.

Comment 5: Conclusion.
Although you mention at the Conclusion some pitfalls of your experiments, I believe there should be a separate paragraph just for the limitations of your experiments, right before the Conclusion, stating in a more concise way the pitfalls, drawbacks and limitations of the experiments.

Comment 6: 2.4 Design of plaque models
How did you decide to fix your experimental models? What influenced you to put:
Fibrous tissue (# = 5%), lipid (# = 20%) and calcium (# = 75%)?

Comment 7: Figure 8
You mention at Fig 8 that you achieved 107mmHg blood pressure. So, all experiments were performed in this blood pressure? Are there results for higher or lower blood pressure?

Comment 8: Figure 10
You state in Fig 10 that you use varying fibrous cap thickness dfc, however from the values there is only a dfc of 0.05mm. Could you please clarify?

Comment 9:
What prompt you to use constant lipid pool (Elp= 1 kPa) and fixed thickness (0.35 mm)?

MINOR ESSENTIAL REVISIONS

Comment 1: 1. Background.
IVUS is an invasive imaging modality and has several limitations for detection of plaque morphology. Certainly it cannot be used for vulnerable plaque detection. However it can be used in the form of VH.

I think there is a mix-up with numbering the paragraphs of the entire chapter 2. For instance, you begin with 2.1 Plaque Composite Model, then 2.2 Plaque Rupture Mechanics, then it follows 2.4 Design of Plaque Models, then there is 2.6 2D Finite Element Method Validation, then comes 2.5 3D Computational Fluid Dynamics Modelling.

Comment 3: 2.5.1 Geometry Reconstruction and Meshing
You talk about ‘inner carotid artery’. I believe the right term is internal carotid artery.

Comment 4: 3.3.1 2D Structural Analysis
‘Highest plague vulnerability’. It is plaque.

Comment 5: 3.4.2 3D Fluid-Structural Analysis
You mention Fig 12. I believe it would be Figure 14. Please also specify what is 14A and 14B in the text.

Comment 6: 4. Conclusion
‘Non-invasive imaging not only identify flow- limiting vascular stenosis, but also to detect calcified and non-calcified plaque, measure atherosclerotic plaque burden and its response to treatment, and to differentiate stable plaques from those which tend to rupture.’ Please correct the grammar in order to achieve a better understanding.

Comment 7:
Did you perform both 2D and 3D experiments in your lab? How many times
each? Did you achieve significant reproducibility of your results?

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests